IN THE UNITED STATES PATENT AND TRADEMARK OFFICE



In re Patent Application of

Elmore et al

Atty. Ref.: 1498-133

Serial No. 08/981,087

Group: 1647

Filed: May 27, 1998

Examiner: Turner

For: TYPE F BOTULINUM TOXIN AND USE THEREOF

January 28, 2003

Assistant Commissioner for Patents Washington, DC 20231

Sir:

STATEMENT

The attached paper and computer readable copies of the Sequence Listing are the same. No new matter has been added.

Respectfully submitted,

NIXON & VANDERHYE P.C.

By:

B. J. Sadoff

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BJS:plb

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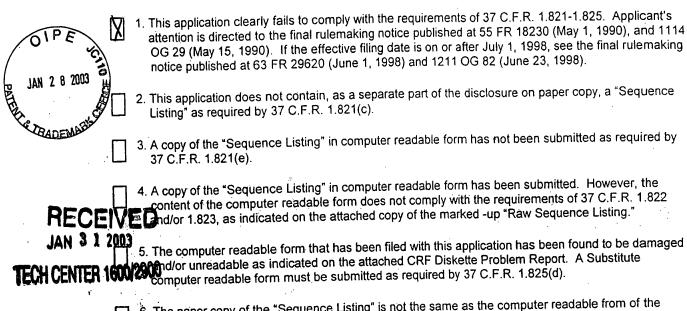
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Applicant must file the items indicated below within the time period set the Office action to which the Notice is attached to avoid abandonment under 35 U.S.C. § 133 (extensions of time may be obtained under the provisions of 37 CFR 1.136(a)).

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):



6. The paper copy of the "Sequence Listing" is not the same as the computer readable from of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).

7. Other: Figure 3 sulleter

Applicant Must Provide:

An initial or <u>substitute</u> computer readable form (CRF) copy of the "Sequence Listing".

An initial or <u>substitute</u> paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification.

A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

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SEQUENCE LISTING

(1) GENERAL INFORMATION:

- (ii) TITLE OF INVENTION: TYPE F BOTULINUM TOXIN AND USE THEREOF
- (iii) NUMBER OF SEQUENCES: 8
- (iv) CORRESPONDENCE ADDRESS:
 - (A) ADDRESSEE: NIXON & VANDERHYE P.C.
 - (B) STREET: 1100 North Glebe Rd. 8th floor
 - (C) CITY: Arlington
 - (D) STATE: VA
 - (E) COUNTRY: USA
 - (F) ZIP: 22201-4741
- (v) COMPUTER READABLE FORM:
 - (A) MEDIUM TYPE: Floppy disk
 - (B) COMPUTER: IBM PC compatible
 - (C) OPERATING SYSTEM: PC-DOS/MS-DOS
 - (D) SOFTWARE: PatentIn Release #1.0, Version #1.30
- (vi) CURRENT APPLICATION DATA:
 - (A) APPLICATION NUMBER: US 08/981,087
 - (B) FILING DATE: 27-MAY-1998
 - (C) CLASSIFICATION:
- (vii) PRIOR APPLICATION DATA:
 - (A) APPLICATION NUMBER: PCT/GB96/01409
 - (B) FILING DATE: 12-JUN-1996
- (vii) PRIOR APPLICATION DATA:
 - (A) APPLICATION NUMBER: GB 9511909.5
 - (B) FILING DATE: 12-JUN-1995
- (viii) ATTORNEY/AGENT INFORMATION:
 - (A) NAME: Crawford, Arthur R.
 - (B) REGISTRATION NUMBER: 25,327
 - (C) REFERENCE/DOCKET NUMBER: 124-688
 - (ix) TELECOMMUNICATION INFORMATION:
 - (A) TELEPHONE: 703-816-4000
 - (B) TELEFAX: 703-816-4100
- (2) INFORMATION FOR SEQ ID NO:1:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 431 amino acids
 - (B) TYPE: amino acid

- (C) STRANDEDNESS:
- (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: peptide
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:1:

Ser Tyr Thr Asn Asp Lys Ile Leu Ile Leu Tyr Phe Asn Lys Leu Tyr 1 5 10 15

Lys Lys Ile Lys Asp Asn Ser Ile Leu Asp Met Arg Tyr Glu Asn Asn 20 25 30

Lys Phe Ile Asp Ile Ser Gly Tyr Gly Ser Asn Ile Ser Ile Asn Gly 35 40 45

Asp Val Tyr Ile Tyr Ser Thr Asn Arg Asn Gln Phe Gly Ile Tyr Ser 50 55 60

Ser Lys Pro Ser Glu Val Asn Ile Ala Gln Asn Asn Asp Ile Ile Tyr 65 70 75 80

Asn Gly Arg Tyr Gln Asn Phe Ser Ile Ser Phe Trp Val Arg Ile Pro 85 90 95

Lys Tyr Phe Asn Lys Val Asn Leu Asn Asn Glu Tyr Thr Ile Ile Asp 100 105 110

Cys Ile Arg Asn Asn Asn Ser Gly Trp Lys Ile Ser Leu Asn Tyr Asn 115 120 125

Lys Ile Ile Trp Thr Leu Gln Asp Thr Ala Gly Asn Asn Gln Lys Leu 130 135 140

Val Phe Asn Tyr Thr Gln Met Ile Ser Ile Ser Asp Tyr Ile Asn Lys 145 150 155 160

Trp Ile Phe Val Thr Ile Thr Asn Asn Arg Leu Gly Asn Ser Arg Ile 165 170 175

Tyr Ile Asn Gly Asn Leu Ile Asp Glu Lys Ser Ile Ser Asn Leu Gly
180 185 190

Asp Ile His Val Ser Asp Asn Ile Leu Phe Lys Ile Val Gly Cys Asn 195 200 205

Asp Thr Arg Tyr Val Gly Ile Arg Tyr Phe Lys Val Phe Asp Thr Glu 210 215 220

Leu Gly Lys Thr Glu Ile Glu Thr Leu Tyr Ser Asp Glu Pro Asp Pro 225 230 235 240

Ser Ile Leu Lys Asp Phe Trp Gly Asn Tyr Leu Leu Tyr Asn Lys Arg 245 250 255

H2

Tyr Tyr Leu Leu Asn Leu Leu Arg Thr Asp Lys Ser Ile Thr Gln Asn 260 265 270

Ser Asn Phe Leu Asn Ile Asn Gln Gln Arg Gly Val Tyr Gln Lys Pro 275 280 285

Asn Ile Phe Ser Asn Thr Arg Leu Tyr Thr Gly Val Glu Val Ile Ile 290 295 300

Arg Lys Asn Gly Ser Thr Asp Ile Ser Asn Thr Asp Asn Phe Val Arg 305 310 315 320

Lys Asn Asp Leu Ala Tyr Ile Asn Val Val Asp Arg Asp Val Glu Tyr 325 330 335

Arg Leu Tyr Ala Asp Ile Ser Ile Ala Lys Pro Glu Lys Ile Ile Lys 340 345 350

Leu Ile Arg Thr Ser Asn Ser Asn Ser Leu Gly Gln Ile Ile Val 355 360 365

Met Asp Ser Ile Gly Asn Asn Cys Thr Met Asn Phe Gln Asn Asn Asn 370 $$ 375 $$ 380

Gly Gly Asn Ile Gly Leu Leu Gly Phe His Ser Asn Asn Leu Val Ala 385 390 395 400

Ser Ser Trp Tyr Tyr Asn Asn Ile Arg Lys Asn Thr Ser Ser Asn Gly 405 410 415

Cys Phe Trp Ser Phe Ile Ser Lys Glu His Gly Trp Gln Glu Asn 420 425 430

(2) INFORMATION FOR SEQ ID NO:2:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 144 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS:
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:2:

Ser Tyr Thr Asn Asp Lys Ile Leu Ile Leu Tyr Phe Asn Lys Leu Tyr 1 5 10 15

Lys Lys Ile Lys Asp Asn Ser Ile Leu Asp Met Arg Tyr Glu Asn Asn 20 25

Lys Phe Ile Asp Ile Ser Gly Tyr Gly Ser Asn Ile Ser Ile Asn Gly 35 40 45

H2

Asp Val Tyr Ile Tyr Ser Thr Asn Arg Asn Gln Phe Gly Ile Tyr Ser 50 55 60

Ser Lys Pro Ser Glu Val Asn Ile Ala Gln Asn Asn Asp Ile Ile Tyr 65 70 75 80

Asn Gly Arg Tyr Gln Asn Phe Ser Ile Ser Phe Trp Val Arg Ile Pro 85 90 95

Lys Tyr Phe Asn Lys Val Asn Leu Asn Asn Glu Tyr Thr Ile Ile Asp 100 105 110

Cys Ile Arg Asn Asn Asn Ser Gly Trp Lys Ile Ser Leu Asn Tyr Asn 115 120 125

Lys Ile Ile Trp Thr Leu Gln Asp Thr Ala Gly Asn Asn Gln Lys Leu 130 135 140

(2) INFORMATION FOR SEQ ID NO:3:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 144 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS:

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:3:

Val Phe Asn Tyr Thr Gln Met Ile Ser Ile Ser Asp Tyr Ile Asn Lys

1 10 15

Trp Ile Phe Val Thr Ile Thr Asn Asn Arg Leu Gly Asn Ser Arg Ile 20 25 30

Tyr Ile Asn Gly Asn Leu Ile Asp Glu Lys Ser Ile Ser Asn Leu Gly 35 40 45

Asp Ile His Val Ser Asp Asn Ile Leu Phe Lys Ile Val Gly Cys Asn 50 60

Asp Thr Arg Tyr Val Gly Ile Arg Tyr Phe Lys Val Phe Asp Thr Glu 65 70 75 80

Leu Gly Lys Thr Glu Ile Glu Thr Leu Tyr Ser Asp Glu Pro Asp Pro 85 90 95

Ser Ile Leu Lys Asp Phe Trp Gly Asn Tyr Leu Leu Tyr Asn Lys Arg 100 105 110

Tyr Tyr Leu Leu Asn Leu Leu Arg Thr Asp Lys Ser Ile Thr Gln Asn

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115 120 125

Ser Asn Phe Leu Asn Ile Asn Gln Gln Arg Gly Val Tyr Gln Lys Pro 130 135 140

- (2) INFORMATION FOR SEQ ID NO:4:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 143 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS:
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: peptide
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:4:

Arg Lys Asn Gly Ser Thr Asp Ile Ser Asn Thr Asp Asn Phe Val Arg 20 25 30

Lys Asn Asp Leu Ala Tyr Ile Asn Val Val Asp Arg Asp Val Glu Tyr 35 40 45

Arg Leu Tyr Ala Asp Ile Ser Ile Ala Lys Pro Glu Lys Ile Ile Lys 50 55 60

Leu Ile Arg Thr Ser Asn Ser Asn Ser Leu Gly Gln Ile Ile Val

Met Asp Ser Ile Gly Asn Asn Cys Thr Met Asn Phe Gln Asn Asn Asn 85 90 95

Gly Gly Asn Ile Gly Leu Leu Gly Phe His Ser Asn Asn Leu Val Ala 100 \$105\$

Ser Ser Trp Tyr Tyr Asn Asn Ile Arg Lys Asn Thr Ser Ser Asn Gly 115 120 125

Cys Phe Trp Ser Phe Ile Ser Lys Glu His Gly Trp Gln Glu Asn 130 135 140

- (2) INFORMATION FOR SEQ ID NO:5:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 1293 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: DNA (genomic)

H2

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:5:

60 TCATATACTA ATGATAAAAT TCTAATTTTA TATTTTAATA AATTATAA AAAAATTAAA GATAACTCTA TTTTAGATAT GCGATATGAA AATAATAAAT TTATAGATAT CTCTGGATAT 120 GGTTCAAATA TAAGCATTAA TGGAGATGTA TATATTTATT CAACAAATAG AAATCAATTT 180 GGAATATATA GTAGTAAGCC TAGTGAAGTT AATATAGCTC AAAATAATGA TATTATATAC 240 300 AATGGTAGAT ATCAAAATTT TAGTATTAGT TTCTGGGTAA GGATTCCTAA ATACTTCAAT AAAGTGAATC TTAATAATGA ATATACTATA ATAGATTGTA TAAGGAATAA TAATTCAGGA 360 TGGAAAATAT CACTTAATTA TAATAAAATA ATTTGGACTT TACAAGATAC TGCTGGAAAT 420 AATCAAAAAC TAGTTTTTAA TTATACACAA ATGATTAGTA TATCTGATTA TATAAATAAA 480 TGGATTTTTG TAACTATTAC TAATAATAGA TTAGGCAATT CTAGAATTTA CATCAATGGA 540 AATTTAATAG ATGAAAAATC AATTTCGAAT TTAGGTGATA TTCATGTTAG TGATAATATA 600 TTATTTAAAA TTGTTGGTTG TAATGATACA AGATATGTTG GTATAAGATA TTTTAAAGTT 660 TTTGATACGG AATTAGGTAA AACAGAAATT GAGACTTTAT ATAGTGATGA GCCAGATCCA 720 780 AATTTACTAA GAACAGATAA GTCTATTACT CAGAATTCAA ACTTTCTAAA TATTAATCAA 840 900 CAAAGAGGTG TTTATCAGAA ACCAAATATT TTTTCCAACA CTAGATTATA TACAGGAGTA 960 GAAGTTATTA TAAGAAAAA TGGATCTACA GATATATCTA ATACAGATAA TTTTGTTAGA AAAAATGATC TGGCATATAT TAATGTAGTA GATCGTGATG TAGAATATCG GCTATATGCT 1020 GATATATCAA TTGCAAAACC AGAGAAAATA ATAAAATTAA TAAGAACATC TAATTCAAAC 1080 1140 AATAGCTTAG GTCAAATTAT AGTTATGGAT TCAATAGGAA ATAATTGCAC AATGAATTTT CAAAACAATA ATGGGGGCAA TATAGGATTA CTAGGTTTTC ATTCAAATAA TTTGGTTGCT 1200 AGTAGTTGGT ATTATAACAA TATACGAAAA AATACTAGCA GTAATGGATG CTTTTGGAGT 1260 1293 TTTATTTCTA AAGAGCATGG ATGGCAAGAA AAC

(2) INFORMATION FOR SEQ ID NO:6:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 1313 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: linear



(xi) SEQUENCE DESCRIPTION: SEQ ID NO:6:

GGATCCATAT	GTCTTACACT	AACGACAAAA	TCCTGATCCT	GTACTTCAAC	AAACTGTACA	60
ААААААТСАА	AGACAACTCT	ATCCTGGACA	TGCGTTACGA	AAACAACAAA	TTCATCGACA	120
TCTCTGGCTA	TGGTTCTAAC	ATCTCTATCA	ACGGTGACGT	CTACATCTAC	TCTACTAACC	180
GCAACCAGTT	CGGTATCTAC	TCTTCTAAAC	CGTCTGAAGT	AAACATCGCT	CAGAACAACG	240
ACATCATCTA	CAACGGTCGT	TACCAGAACT	TCTCTATCTC	TTTCTGGGTT	CGTATCCCGA	300
AATACTTCAA	CAAAGTTAAC	CTGAACAACG	AATACACTAT	CATCGACTGC	ATCCGTAACA	360
ACAACTCTGG	TTGGAAAATC	TCTCTGAACT	ACAACAAAAT	CATCTGGACT	CTGCAGGACA	420
CTGCTGGTAA	CAACCAGAAA	CTGGTTTTCA	ACTACACTCA	GATGATCTCT	ATCTCTGACT	480
ACATTAATAA	ATGGATCTTC	GTTACTATCA	CTAACAACCG	TCTGGGTAAC	TCTCGTATCT	540
ACATCAACGG	TAACCTGATC	GATGAAAAAT	CTATCTCTAA	CCTGGGTGAC	ATCCACGTTT	600
CTGACAACAT	CCTGTTCAAA	ATCGTTGGTT	GCAACGACAC	GCGTTACGTT	GGTATCCGTT	660
ACTTCAAAGT	TTTCGACACT	GAACTGGGTA	AAACTGAAAT	CGAAACTCTG	TACTCTGACG	720
AACCGGACCC	GTCTATCCTG	AAAGACTTCT	GGGGTAACTA	CCTGCTGTAC	AACAAACGTT	780
ACTACCTGCT	GAACCTGCTC	CGGACTGACA	AATCTATCAC	TCAGAACTCT	AACTTCCTGA	840
ACATCAACCA	GCAGCGTGGT	GTTTATCAGA	AACCTAATAT	CTTCTCTAAC	ACTCGTCTGT	900
ACACTGGTGT	TGAAGTTATC	ATCCGTAAAA	ACGGTTCTAC	TGACATCTCT	AACACTGACA	960
ACTTCGTACG	TAAAAACGAC	CTGGCTTACA	TCAACGTTGT	TGACCGTGAC	GTTGAATACC	1020
GTCTGTACGC	TGACATCTCT	ATCGCTAAAC'	CGGAAAAAAT	CATCAAACTG	ATCCGTACTT	1080
СТААСТСТАА	CAACTCTCTG	GGTCAGATCA	TCGTTATGGA	CTCGATCGGT	AACAACTGCA	1140
CTATGAACTT	CCAGAACAAC	AACGGTGGTA	ACATCGGTCT	GCTGGGTTTC	CACTCTAACA	1200
ACCTGGTTGC	TTCTTCTTGG	TACTACAACA	ACATCCGTAA	AAACACTTCT	TCTAACGGTT	1260
GCTTCTGGTC	TTTCATCTCT	AAAGAACACG	GTTGGCAGGA	AAACTAATCT	AGA	1313

(2) INFORMATION FOR SEQ ID NO:7:

HZ

⁽i) SEQUENCE CHARACTERISTICS:

⁽A) LENGTH: 57 base pairs

- (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:7:

ATCGAGGGAA GGATTTCAGA ATTCGGATCC TCTAGAGTCG ACCTGCAGGC AAGCTTG

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- (2) INFORMATION FOR SEQ ID NO:8:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 5 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

- (ii) MOLECULE TYPE: peptide
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:8:

Ile Glu Gly Arg Ile